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10/582,687	06/13/2006	Pasqua Anna Oreste	GRT/3687-177	2203
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ARLINGTON, VA 22203				
EXAMINER				
BLAND, LAYLA D				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/582,687

Applicant(s)

ORESTE ET AL.

Examiner

LAYLA BLAND

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 1-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-21, 23-25 and 27 is/are rejected.
- 7) ☐ Claim(s) 22 and 26 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

3DETAILED ACTION

This office action is a response to Applicant's amendment submitted January 12, 2009, wherein claims 28-35 are canceled.

Claims 1-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 17-27 are examined on the merits herein.

In view of Applicant's remarks submitted January 12, 2009, the rejection of claims 22 and 26 under 35 USC 103(a) as being unpatentable over Oreste et al. in view of Naggi et al. is withdrawn. Applicant's arguments are persuasive. The oversulfation and desulfation steps performed in the examples given in the instant specification were done under the same conditions as Example 1 of the Oreste reference. In the instant case, depolymerization was carried out before the oversulfation and desulfation while the depolymerization was carried out as the last step in the Oreste reference. The sulfur content in glucosamine 3-O-sulfate in the instant example is significantly higher than the sulfur content in glucosamine 3-O-sulfate in the Oreste example, although the reactions were carried out under the same conditions. Thus, this unexpected result is evidence of non-obviousness as to claims 22 and 26.

The provisional rejection of claims 17-27 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 35-62 of copending Application No. 09/950,003 is withdrawn because copending Application No. 09/950,003 is now abandoned. A rejection was not made over copending Application

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No. 12/198,426, continuation of Application No. 09/950,003, because the claims of copending Application No. 12/198,426 do not recite the claimed structure (a') and do not recite products prepared via nitrous acid depolymerization and treatment with sodium borohydride, which would produce products having the structure (a').

The following rejections are maintained:

Claim Rejections - 35 USC § 103

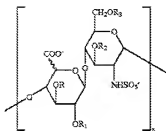
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-21, 23-25, and 27 are rejected under 35 U.S.C. 103(a) as obvious over Oreste et al. (WO 02/50125, June 27, 2002, PTO-1449 submitted June 13, 2006).

Oreste et al. teach glycosaminoglycans derived from K5 polysaccharides [see abstract] which consist of a mixture of chains in which at least 90% of said chains have the formula

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, wherein 40-60% of the uronic acid units are iduronic acid, the sulfation degree is 2.3 to 2.9, R_3 is 85% to 95% SO_3^- , R_2 is 17-21% SO_3^- , R_1 is about 15-35% SO_3^- in iduronic units and 0-5% SO_3^- in glucuronic units, R is from 20-40% SO_3^- in glucuronic units and 0-5% in iduronic units, and the mean molecular weight is from about 6,000 to about 8,000 [claims 25 and 31]. In one embodiment, n is from 3 to 15 [claim 29]. Oreste et al. also teach pharmaceutical compositions comprising these compounds and pharmaceutically acceptable carriers [claim 38]. The compounds have high antithrombin activity and are useful for the control of coagulation [see abstract].

Oreste et al. are silent on the structure at the reducing end of the majority of the chains. However, the skilled artisan would understand that compounds made by the methods of Oreste et al., wherein the compounds are depolymerized early in the synthesis via nitrous acid depolymerization and reaction with sodium borohydride [page 14, lines 27-31 and page 15, lines 1-6] would necessarily have the claimed sulfated structure at the reducing end of the majority of the chains. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195

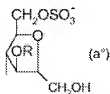
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USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Claims 17 and 33-25 are product-by process claims. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.). See MPEP 2113. The limitation "depolymerized" is also interpreted as drawn to the method of production, which results in a low molecular weight product.

Response to Arguments

Applicant argues that the process described in WO 02/50125 results in a product having the following structure at the reducing end of the majority of the chains:



The difference between this structure and the claimed one is that the claimed structure is sulfated (has $\text{CH}_2\text{OSO}_3^-$ in place of CH_2OH). The above structure results from nitrous depolymerization followed by treatment with sodium borohydride at the end of the synthesis, as taught by Oreste et al. [see page 30, Example 2]. Nitrous depolymerization and sodium borohydride treatment are known reactions, referenced by Oreste et al. to WO 82/03627, and the results of these reactions can be predicted by the skilled artisan. Thus, processes taught by Oreste wherein depolymerization occurs as the final step do not anticipate the claims. However, Oreste et al. teach that the depolymerization may be carried out early in the synthesis. If the depolymerization is carried out early in the synthesis, before the sulfation steps taught on page 3 of Oreste, the structure at the end of the chains would be subject to sulfation and the skilled artisan would expect to achieve the claimed sulfated product.

Applicant argues that the starting materials used to prepare the product of claim 17, prepared by nitrous depolymerization, were not known in the prior art. This argument is not persuasive because Applicant's starting material is the product which the skilled artisan would achieve if he or she carried out nitrous depolymerization on Oreste's product of step (ii), which was suggested by Oreste [page 7, lines 12-14]. Oreste's product of step (ii) is N-deacylated and N-sulfated and epimerized; after being subjected to nitrous acid depolymerization, that product is a depolymerized-LMW-epiK5-N,O-sulfate, which is the starting material in claim 17. It is noted that, if the skilled artisan then continued Oreste's process through step (vi), including the steps of

oversulfation, selective O-desulfation, selective 6-O-sulfation, and N-sulfation, he or she would carry out the process recited in claim 17 and realize the same product.

Applicant argues that the Examiner did not address the scope of the prior art, the level of ordinary skill in the art, and the differences between the claimed invention and the prior art. The level of ordinary skill in the art is presumed to be an ordinary organic chemist. The scope of the prior art and the differences between the claimed invention and the prior art are set forth above. Applicant argues that no rational basis was made for modifying WO 02/50125. The basis for modifying WO 02/50125 such that the depolymerization occurs early in the synthesis instead of at the end, thereby producing the claimed products, is found in the reference itself, as set forth above.

In response to applicant's argument that the claimed properties have advantageous properties compared to Oreste's products, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicant argues that the claimed compounds have unexpected properties. As set forth in the previous office action, MPEP 2145 states: "If a *prima facie* case of obviousness is established, the burden shifts to the applicant to come forward with arguments and/or evidence to rebut the *prima facie* case," and "the evidence must be reasonably commensurate in scope with the claimed invention." The compound of Example 1 has a sulfation degree of 2.83 and a content of 95-100% in N-sulfated

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glucosamine, 80% in 6-O-sulfated glucosamine, 50% in 3-O-sulfated glucosamine, 40% in 3-O-sulfated glucuronic acid and 20% in 2-O-sulfated iduronic acid. Claims 17-21, 23-24, and 27 are drawn to a broad genus of compounds, of which Example 1 is a member, but Example 1 is not representative of the broad genus. For example, Example 1 has a sulfation degree of 2.83, at one end of the range 2.3-2.9 recited in claim 17. Example 1 is also drawn to products having specific content in N-sulfated glucosamine, 3-O-sulfated glucosamine, 3-O-sulfated glucuronic acid and in 2-O-sulfated iduronic acid, and claim 17 is not limited at all in those respects. For these reasons, Applicant's argument is not persuasive.

Claims 22 and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/Layla Bland/
Examiner, Art Unit 1623